

REMARKS

Claims 1, 2, 4, 8, 12, 13, 15, 17, 20, 28, 29, 31, 33, 34, 36, 39-41, 46, 49, 51, 61, 62, 64, 66, 67 and 69-78 are pending in the application. Claims 1, 2, 4, 8, 12, 13, 15, 17, 20 and 28 have been withdrawn. Claims 29, 33, 61 and 62 have been amended. Claims 63 and 64 have been cancelled. Claim 78 has been added.

Claims 29, 31, 33, 36, 39-41, 46, 49, 51, 61, 62, 64, 66, 67 and 69-77 were rejected under 35 U.S.C. § 112 as being indefinite. Those claims, which comprise independent Claims 29 and all others depending therefrom (including new Claim 78), have been amended to define the fat and oil substance of the claimed composition as a component. As such, the 35 U.S.C. § 112 rejection should be withdrawn.

The pending claims which were not withdrawn were rejected under 35 U.S.C. 103(a) as being unpatentable over Chopra in view of Motoyama et al. For the reasons hereinafter recited, applicant's respectfully submit that independent Claim 29 (and its dependent claims), as amended, should now be in allowable form.

The invention of Claim 29 et seq. relates to a composition which comprises reduced coenzyme Q₁₀, a polyglycerol fatty acid ester and a fat and oil component and/or a polyol, wherein the content of vitamin E (when the same is further contained in the composition) is lower than 4% by weight based on total weight of the composition minus a weight of coenzyme Q₁₀, and wherein the content of Tween and/or Span species (when the same is further contained in the composition) is not higher than 30% by weight based on total weight of the composition minus the weight of coenzyme Q₁₀.

The composition of the claimed invention can have the good stability of reduced coenzyme Q₁₀ and, simultaneously, have high-level absorbability in the living body. This is described on page 4, line 35 – page 5, line 24 in the specification. First, the inventors found that reduced coenzyme Q₁₀ is protected against oxidation by molecular oxygen and stabilized in a surprisingly favorable manner in the presence of a fat and oil component and/or a polyol without preparing any complicated and otherwise troublesome composition. Second, the inventors also found that while the addition of

Tween and Span species (surfactants, emulsifiers) in wide use markedly decrease the above-mentioned reduced coenzyme Q₁₀ stabilizing effect of a fat and oil component and/or polyol, the addition of polyglycerol fatty acid esters surprisingly has little influence on the stabilizing effect of the fat and oil component and/or polyol, and such esters serve as very favorable surfactants (emulsifiers). Specifically, the addition of the polyglycerol fatty acid ester enhances absorbability of reduced coenzyme Q₁₀ in the living body without inhibiting the reduced coenzyme Q₁₀ stabilizing effect of the fat and oil component and/or polyol so that reduced coenzyme Q₁₀ can be stably maintained.

In contrast to the claimed invention, Chopra relates to a composition comprising ubiquinol and an amount of a reducing agent effective to reduce or eliminate the oxidation of said ubiquinol to ubiquinone. That composition further comprises an amount of a surfactant or vegetable oil or mixtures thereof and, optionally, a solvent effective to solubilize the ubiquinol and the reducing agent.

As the Examiner recognizes, Chopra does not disclose the reduced coenzyme Q₁₀-containing composition comprising the polyglycerol fatty acid ester of the claimed invention. In addition, the components other than the polyglycerol fatty acid ester in the composition of the present invention are also different from those in Chopra.

Since the composition of Chopra contains a large quantity of Vitamin E or Tween/Span, the composition cannot stably maintain reduced coenzyme Q₁₀ without a reducing agent. This is clear from the results of Examples 18-19 and Comparative Examples 3-4 and from the results of Examples 20-22 and Comparative Examples 5-8 in the present specification. Thus, the composition of Chopra stably maintains reduced coenzyme Q₁₀ by using a reducing agent. On the other hand, by incorporating the fat and oil component and/or the polyol, the composition of the claimed present invention can stably maintain reduced coenzyme Q₁₀ whether the composition contains a reducing agent or not.

As shown in the attached Declaration of Takihiro Ueda, the present invention can stably maintain reduced coenzyme Q₁₀ without using a large amount of reducing agent,

even though Chopra requires the use of a large amount of reducing agent in order to stably maintain reduced coenzyme Q₁₀. As is clear from the Experiment 1, the composition containing not higher than 30% by weight of Tween80 showed high stability of reduced coenzyme Q₁₀, but the composition containing not higher than 30% by weight of Tween80 substantially inhibited the stability of reduced coenzyme Q₁₀. Thus, when the composition contains higher than 30% by weight of Tween and/or Span, the stability of reduced coenzyme Q₁₀ is different based on the amount of reducing agent used. On the other hand, when the composition contains no higher than 30% by weight of Tween and/or Span, the stability of reduced coenzyme Q₁₀ does not depend on the amount of reducing agent used, and reduced coenzyme Q₁₀ can be stably maintained. However, Chopra neither discloses nor suggest the composition and the excellent effects of the present invention. Therefore, Chopra neither discloses nor suggests that the composition of the present invention can stably maintain reduced coenzyme Q₁₀ by using a fat and oil component and/or the polyol. Furthermore, Chopra neither discloses nor suggests that the addition of the polyglycerol fatty acid ester enhances absorbability of reduced coenzyme Q₁₀ in the living body without inhibiting the reduced coenzymeQ₁₀-stabilising effect of the fat and oil component and/or polyol.

Motoyama et al., on the other hand, relates to a pharmaceutical composition which provides a high degree of bioavailability of cyclandelate when administered orally. The composition consists of a mixture of (a) a polyglycerol ester of an unsaturated fatty acid or mixtures thereof and (b) cyclandelate. Motoyama et al. only describes coenzyme Q₁₀ (ubidecarenone: oxidized coenzyme Q₁₀) on column 2, lines 55-56, and does not describe reduced coenzyme Q₁₀. Thus, since Motoyama et al. uses coenzyme Q₁₀ (which is already oxidized), Motoyama et al. does not intend to maintain reduced coenzyme Q₁₀ stable at all. Furthermore, Motoyama et al. neither discloses nor suggests the effects of the present invention in which reduced coenzyme Q₁₀ is stabilized in the presence of a fat and oil component and/or polyol and the addition of the polyglycerol fatty acid ester hardly inhibits the reduced coenzyme Q₁₀-stabilizing effect of the fat and oil component and/or polyol.

As discussed above, the components other than the polyglycerol fatty acid ester in the composition of the present invention also differ from those in Chopra. Even if Chopra and Motoyama et al. are combined, the specific composition of the claimed invention could not be is unobvious from the combination. The combination would not suggest that the combined could have the good stability of reduced coenzyme Q₁₀ and simultaneously have the high-level absorbability in the living body of the present invention.

With respect to the obviousness-type double patenting rejection, amended Claim 29 contains the limitations of contents of vitamin E and Tween and/or Span. On the other hand, Claim 16 of co-pending application 11/586,511 does not have these limitations. Therefore, it is submitted that the obviousness-type double patenting rejection should be withdrawn.

Applicants respectfully submit that amended Claim 29 and its pending dependent claims should now be in condition for allowance. Passage of the application to issue is requested.

Respectfully submitted,

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Attachment: Declaration of
Takahiro Ueda

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Yasuyoshi Ueda et al.

Serial No.: 10/501,698

Art Unit: 1657

Filed: February 3, 2005

Examiner: Satyendra K. Singh

Title: METHOD FOR STABILIZING REDUCED COENZYME Q₁₀ AND
COMPOSITION THEREFOR

DECLARATION UNDER RULE 132

Honorable Commissioner of Patents and Trademarks,
Alexandria, Virginia 22313-1450

Sir:

I, Takahiro Ueda, a citizen of Japan and having postal mailing address of 6-31-17-2018, Shioya-cho, Tarumi-ku, Kobe-shi, Hyogo 655-0872 JAPAN, declare and say that:

March, 2000, I was graduated from Kobe University Graduate School of Science and Technology, and received a Master Degree in chemistry;

Since April, 2000, I have been employed by Kaneka Corporation, and engaged in the works of research and development for fine chemicals in Functional Food Ingredient Division, Healthcare Products Business Unit;

I am one of the inventors of the above-identified application and am familiar with the subject matter thereof;

I have read the Official Action mailed and the references cited therein and I am familiar with the subject matter thereof;

I respectfully submit herewith my exact report thereon;

Experiment

The following additional Experiment was conducted.

<Experiment 1>

MCT and Tween80 (total weight 5 g), which were prepared to have the weight ratio shown in Table 1, were poured into a 50 mL bottle. To the bottle, 0.3 g of the crystals (reduced coenzyme Q₁₀) obtained in Production Example 2 in the present specification and 7 mg of ascorbyl palmitate were added. The resulting mixtures were stored in the air at 60°C for 60 hours, and the reduced coenzyme Q₁₀/oxidized coenzyme Q₁₀ weight ratios in the solutions were determined. The results are shown in Table 1.

Table 1

Weight ratio of MCT/Tween80	Content of Tween80 *	R
90/10	10.0	95.2/4.8
80/20	20.0	96.1/3.9
70/30	30.0	94.7/5.3
60/40	39.9	89.9/10.1
50/50	49.9	87.9/12.1


*: content of Tween80 based on the system excluding coenzyme Q₁₀ (% by weight)

R: reduced coenzyme Q₁₀/oxidized coenzyme Q₁₀ weight ratio

From the results shown in Table 1, it is clear that the stabilization of reduced coenzyme Q₁₀ is not inhibited when the content of Tween80 is not higher than 30% by weight based on the system excluding coenzyme Q₁₀.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signed this 17th day of March, 2009


Takahiro Ueda